3.4 POTENCY EQUIVALENCE FACTORS

One approach used to assess the cancer risk of mixtures of structurally related compounds such as PAHs is to characterize the toxicities of these compounds relative to the toxicity of a compound representative of the group. This is known as the potency equivalence factors (PEFs) approach and it takes into account the differing potencies of carcinogenic compounds from structurally related mixtures. This weighting scheme for PAHs was developed by the Air Toxicology and Epidemiology Section of the Office of Environmental Health Hazard Assessment in the document entitled *Health Effects of Benzo(a)pyrene* (Cal/EPA 1993).

The PEF values presented in Table 3-3 may be used for both inhalation and oral exposure pathways, although data used for their development were prioritized so inhalation exposure received higher priority than did other exposures. The benzo(a)pyrene CSF was multiplied by the appropriate chemical-specific PEF value to derive oral and inhalation toxicity values. The COPCs for which this process was conducted are noted in Table 3-2.

TABLE 3-3
POTENCY EQUIVALENCE FACTORS (PEFs) FOR POLYAROMATIC HYDROCARBONS (PAHs)

PAH or Derivative	CAS No.	Suggested PEF
benzo(a)pyrene (index compound)*	50-32-8	1.0
1,6-dinitropyrene	42397-64-8	10
1,8-dinitropyrene	42397-65-9	1.0
1-nitropyrene	5522-43-0	0.1
2-nitrofluorene	607-57-8	0.01
4-nitropyrene	57835-92-4	0.1
5-methylchrysene	3697-24-3	1.0
6-nitrocrysene	7496-02-8	10
7H-dibenzo(c,g)carbazole	194-59-2	1.0
benzo(a)anthracene*	56-55-3	0.1
benzo(b)fluoranthene*	205-99-2	0.1

TABLE 3-3
POTENCY EQUIVALENCE FACTORS (PEFs) FOR
POLYAROMATIC HYDROCARBONS (PAHs)
(CONTINUED)

PAH or Derivative	CAS No.	Suggested PEF
benzo(j)fluoranthene	205-82-3	0.1
benzo(k)fluoranthene*	207-08-9	0.1
chrysene*	218-01-9	0.01
dibenz(a,h)acridine	226-36-8	0.1
dibenz(a,j)acridine	224-42-0	0.1
dibenzo(a,e)pyrene	192-65-4	1.0
dibenzo(a,h)pyrene	189-64-0	10
dibenzo(a,i)pyrene	189-55-9	10
dibenzo(a,l)pyrene	191-30-0	10
indeno(1,2,3-c,d)pyrene*	193-39-5	0.1

*Parcel A COPC

SOURCE:
Health Effects of Benzo(a)pyrene (Cal/EPA 1993)

3. TOXICITY ASSESSMENT

The objective of this section is to provide information on the toxic effects of exposure to constituents. More specifically, the section provides a quantitative estimate of the relationship between exposure and severity or probability of human biological effects for each constituent of potential concern (COPC) identified in Section 2.

Section 3.1 describes how toxicity values are established and used for noncarcinogenic COPCs, while Section 3.2 presents a similar discussion of carcinogenic COPCs. Section 3.3 describes how dermal exposures are quantified.

Relevant carcinogenic and noncarcinogenic toxicity data were obtained from the following sources (in descending order of preference):

1. California Cancer Potency Factors Update (Cal/EPA 1996)
2. Integrated Risk Information System (IRIS) on-line database (EPA 1997a)
3. Health Effects Assessment Summary Tables (HEAST) for FY 1997 (EPA 1997b)
4. Cal/EPA Potency Equivalency Factors for Poly-Aromatic Hydrocarbons (Cal/EPA 1993)
5. Surrogate values provided by DTSC/HERD (Cal/EPA 1998)

Searches of the IRIS database were made in January 1998.

3.1 NONCARCINOGENIC CONSTITUENTS

For the noncarcinogenic effects of constituents, EPA assumes a dose exists below which no adverse health effects will be seen (EPA 1989a). Below this "threshold," it is believed exposure to a constituent can be tolerated without adverse effects, and the body burden is not increased.

Toxic effects become manifest only when physiologic protective mechanisms are overcome by exposure doses above the threshold.

The reference dose (RfD), expressed in units of milligrams per kilogram-day (mg/kg-d), represents the daily intake (averaged over a year) of a constituent per kilogram of body weight which is below the effect threshold for that constituent. In essence, the RfD represents the receptor-specific threshold dose. In addition, EPA assumes noncarcinogenic exposure doses are not cumulative from age group to age group over a lifetime of exposure (EPA 1989a). An RfD is specific to the constituent, route of exposure, and duration over which the exposure occurs.

The EPA reviews all relevant human and animal studies for each constituent and selects the studies pertinent to the derivation of specific RfDs. Each study is evaluated to determine the no-observable-adverse-effect level (NOAEL) or, if data are inadequate for such a determination, the lowest-observable-adverse-effect level (LOAEL). The NOAEL corresponds to the dose (mg/kg-d) that can be administered over a lifetime without inducing observable adverse effects. The LOAEL corresponds to the lowest daily dose (mg/kg-d) that can be administered over a lifetime that induces an observable adverse effect. The toxic effect characterized by the LOAEL is referred to as the "critical effect" (EPA 1997a).

To derive an RfD, the NOAEL (or LOAEL) is divided by uncertainty factors to ensure that the RfD will be protective of human health. Uncertainty factors are applied to account for: 1) extrapolation of data from laboratory animals to humans (interspecies extrapolation), 2) variation in human sensitivity to the toxic effects of a constituent (intraspecies differences), 3) derivation of a chronic RfD based on a subchronic rather than a chronic study, and 4) derivation of an RfD from the LOAEL rather than the NOAEL. Each of these uncertainties usually represents a factor of 10. In addition to these uncertainty factors, modifying factors between 0 and 10 may be applied to reflect additional qualitative considerations in evaluating the data (EPA 1989a).

The inhalation and oral RfDs for the noncarcinogenic COPCs at Parcel A are presented in Table 3-1. The primary source for toxicological reference values is the IRIS on-line database (EPA

1997a), which contains current health risk and regulatory information. Provisional RfDs are tabulated in HEAST (EPA 1997b). When values were not available from the above-mentioned sources, surrogate values were provided by DTSC/HERD, as noted in Table 3-1 (Cal/EPA 1998).

TABLE 3-1
COPC-SPECIFIC REFERENCE DOSE VALUES*

COPC	Subchronic Inhalation RfD (mg/kg-d)	Chronic Inhalation RfD (mg/kg-d)	Subchronic Oral RfD (mg/kg-d)	Chronic Oral RfD (mg/kg-d)
1,1-dichloroethene	9.00E-03	9.00E-03	9.00E-03	9.00E-03
1,2,4-trimethylbenzene	2.00E-03	2.00E-03	5.00E-01	5.00E-01
1,3,5-trimethylbenzene	2.00E-03	2.00E-03	5.00E-01	5.00E-01
aroclor 1248	7.00E-05	7.00E-05	7.00E-05	7.00E-05
aroclor 1254	7.00E-05	7.00E-05	7.00E-05	7.00E-05
aroclor 1260	7.00E-05	7.00E-05	7.00E-05	7.00E-05
arsenic	3.00E-04	3.00E-04	3.00E-04	3.00E-04
benzo(a)anthracene	4.00E-02	4.00E-02	4.00E-02	4.00E-02
benzo(a)pyrene	4.00E-02	4.00E-02	4.00E-02	4.00E-02
benzo(b)fluoranthene	4.00E-02	4.00E-02	4.00E-02	4.00E-02
benzo(k)fluoranthene	4.00E-02	4.00E-02	4.00E-02	4.00E-02
bis(2-ethylhexyl)phthalate	2.00E-02	2.00E-02	2.00E-02	2.00E-02
chrysene	4.00E-02	4.00E-02	4.00E-02	4.00E-02
dibenzo(a,h)anthracene	4.00E-02	4.00E-02	4.00E-02	4.00E-02
fluoranthene	4.00E-01[b]	4.00E-02[a]	4.00E-01[b]	4.00E-02[a]
indeno(1,2,3-cd)pyrene	4.00E-02	4.00E-02	4.00E-02	4.00E-02
naphthalene	4.00E-02[b]	4.00E-02[a]	4.00E-02[b]	4.00E-02[a]
n-butylbenzene	2.90E-01	2.90E-01	1.00E-01	1.00E-01
n-propylbenzene	2.90E-01	2.90E-01	1.00E-01	1.00E-01
p-cymene	1.00E-01	1.00E-01	1.00E-01	1.00E-01
phenanthrene	3.00E-01	3.00E-01	3.00E-01	3.00E-01
pyrene	3.00E-01[b]	3.00E-02[b]	3.00E-01[b]	3.00E-02[a]
tetrachloroethylene	1.00E-01[b]	1.00E-02[b]	1.00E-01[b]	1.00E-02[a]
trichloroethene	7.35E-03	7.35E-03	7.35E-03	7.35E-03
xylenes	2.00E-01	2.00E-01	2.00E+00[b]	2.00E+00[a]

SOURCES:
*DTSC/HERD Surrogate RfD Values (Cal/EPA 1998) except as noted.
[a]IRIS (EPA 1997a)
[b]HEAST (EPA 1997b)

The noncarcinogenic risk associated with a constituent exposure is expressed as the *hazard quotient* (HQ). The HQ is a ratio of the estimated constituent intake, based on the measured or calculated exposure concentration for a constituent (dose), divided by the appropriate oral or inhalation RfD. If the HQ exceeds 1, some harmful effect may occur or the threshold dose may be exceeded. If the HQ is equal to or less than 1, the exposure level is not likely to cause adverse effects. If exposure to multiple constituents occurs, the potential for harmful effects is assessed by summing the HQs and is designated the *hazard index* (HI).

In keeping with EPA guidance (EPA 1989a), all noncarcinogenic risk was considered additive for individual receptors. Since the noncarcinogenic COPCs under investigation at the site are associated with various adverse effects on distinct target organs and systems, the assumption of additivity of effects may overstate the potential for harmful effects. On the other hand, the potential synergistic effects of two or more COPCs must also be recognized. That is, the combined effects of exposure to two COPCs may be worse than exposure to either COPC alone because of interactions.

3.2 CARCINOGENIC CONSTITUENTS

The incremental lifetime cancer risk (ILCR) from a carcinogen is calculated as a product of the reasonable maximum daily intake (mg/kg-d) and the cancer slope factor (CSF). EPA's model of carcinogenesis assumes the relationship between exposure to a carcinogen and cancer risk is linear over the entire dose range, except at very high doses (EPA 1989a). This linearity assumes that there is no threshold-of-exposure dose below which harmful effects will not occur. Because of this, carcinogenic effects are considered to be cumulative across age groups when considering lifetime exposures.

CSFs are upper-bound (95 percent upper confidence limit [UCL]) estimates of the increased cancer risk per unit dose, in which risk is expressed as the probability that an individual will develop cancer within his or her lifetime as the result of exposure to a given level of a

carcinogen. All cancers or tumors are considered whether or not death occurs as a result. This approach is inherently conservative because of the no-threshold assumption and the use of the 95 percent UCL of the estimated slope of dose versus cancer risk.

In addition to the CSF, the toxicity information considered in the assessment of potential carcinogenic risks includes a weight-of-evidence classification. As discussed in Section 2.3, EPA groups constituents according to their potential for carcinogenic effects based on clinical evidence (EPA 1989a):

- Group A Human carcinogen
- Group B Probable human carcinogen
- Group C Possible human carcinogen
- Group D Insufficient data to classify as a human carcinogen
- Group E Not a human carcinogen

The CSFs for the COPCs studied in this report are presented in Table 3-2. The primary source for toxicological reference values is the California Cancer Potency Factors Update (Cal/EPA 1996), followed by IRIS (EPA 1997a). Provisional CSFs are tabulated in HEAST (EPA 1997b). Surrogate values were provided by DTSC/HERD when not available through the previously mentioned sources (Cal/EPA 1998). These values have been noted in Table 3-2. By agreement between DTSC/HERD and Integrated, 1,1-dichloroethene will not be assessed for carcinogenic risk. This agreement is based on DTSC/HERD's review of the 1,1-dichloroethene CSF and supporting toxicological data (Cal/EPA 1998, IESI 1998b).

3.3 Quantification of Dermal Exposure Risks

Dermal RfDs and CSFs are traditionally derived from the corresponding oral values (EPA 1989a). However, DTSC recommends that dermal RfDs and CSFs should not be derived; instead, oral RfDs and CSFs should be used to estimate dermal toxicity values (Cal/EPA 1998b, 1998c).

TABLE 3-2
COPC-SPECIFIC CANCER SLOPE FACTORS (CSFs)*

COPC	Oral CSF 1/(mg/kg-d)	Inhalation CSF 1/(mg/kg-d)
1,1-dichloroethene[a]	NA	NA
1,2,4-trimethylbenzene[a]	NA	NA
1,3,5-trimethylbenzene[a]	NA	NA
aroclor 1248	7.70E+00	7.70E+00
aroclor 1254	7.70E+00	7.70E+00
aroclor 1260	7.70E+00	7.70E+00
arsenic	1.50E+00	1.20E+01
benzo(a)anthracene[b]	1.15E+00	3.90E-01
benzo(a)pyrene	1.15E+01	3.90E+00
benzo(b)fluoranthene[b]	1.15E+00	3.90E-01
benzo(k)fluoranthene[b]	1.15E+00	3.90E-01
bis(2-ethylhexyl)phthalate	8.40E-03	8.40E-03
chrysene[b]	1.15E-01	3.90E-02
dibenzo(a,h)anthracene	4.10E+00	4.10E+00
fluoranthene	NA	NA
indeno(1,2,3-cd)pyrene[b]	1.15E+00	3.90E-01
naphthalene	NA	NA
n-butylbenzene[a]	NA	NA
n-propylbenzene[a]	NA	NA
p-cymene[a]	NA	NA
phenanthrene[a]	NA	NA
pyrene	NA	NA
tetrachloroethylene	5.10E-02	2.10E-02
trichloroethene	1.50E-02	1.00E-02
xylenes	NA	NA

NA = Not Applicable

SOURCES:
*California Cancer Potency Factors Update (Cal/EPA 1996) except as noted.
[a]DTSC/HERD surrogate CSF values (Cal/EPA 1998)
[b]Based on PEF adjustment (see Section 3.4, below).